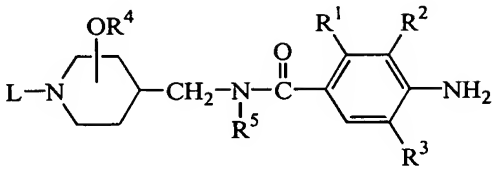
Claims

1. A compound of formula (I)



(I),

a stereochemically isomeric form thereof, an *N*-oxide form thereof or a pharmaceutically acceptable acid or base addition salt thereof, wherein

R^1 and R^2 taken together form a bivalent radical of formula

-O-CH_2-O- (a-1),

-O-CH_2-CH_2- (a-2),

-O-CH_2-CH_2-O- (a-3),

-O-CH_2-CH_2-CH_2- (a-4),

-O-CH_2-CH_2-CH_2-O- (a-5),

-O-CH_2-CH_2-CH_2-CH_2- (a-6),

wherein in said bivalent radicals one or two hydrogen atoms may be substituted with C_{1-6}alkyl,

R^3 is hydrogen or halo;

R^4 is hydrogen or C_{1-6}alkyl;

R^5 is hydrogen or C_{1-6}alkyl;

L is C_{3-6}cycloalkyl, C_{5-6}cycloalkanone, or C_{2-6}alkenyl,

or L is a radical of formula

-Alk-R^6 (b-1),

-Alk-X-R^7 (b-2),

-Alk-Y-C(=O)-R^9 (b-3), or

-Alk-Y-C(=O)-$NR^{11}R^{12}$ (b-4),

wherein each Alk is C_{1-12}alkanediyl; and

R^6 is hydrogen, hydroxy, cyano, C_{1-6}alkylsulfonylamino, C_{3-6}cycloalkyl, C_{5-6}cycloalkanone, or Het^1;

R^7 is hydrogen, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{3-6}cycloalkyl, or Het^2;

X is O, S, SO_2 or NR^8; said R^8 being hydrogen or C_{1-6}alkyl;

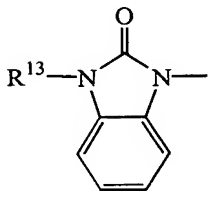
R^9 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{1-6}alkyloxy or hydroxy;

Y is NR^{10} or a direct bond; said R^{10} being hydrogen or C_{1-6}alkyl;

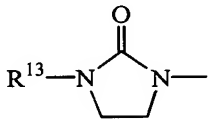
R^{11} and R^{12} each independently are hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, or R^{11} and R^{12} combined with the nitrogen atom bearing R^{11} and R^{12} may form a

pyrrolidinyl or piperidinyl ring both being optionally substituted with C_{1-6}alkyl, amino or mono or di(C_{1-6}alkyl)amino, or said R^{11} and R^{12} combined with the nitrogen bearing R^{11} and R^{12} may form a piperazinyl or 4-morpholinyl radical both being optionally substituted with C_{1-6}alkyl; and Het^1 and Het^2 each independently are selected from furan; furan substituted with C_{1-6}alkyl or halo; tetrahydrofuran; a tetrahydrofuran substituted with C_{1-6}alkyl; a dioxolane; a dioxolane substituted with C_{1-6}alkyl, a dioxane; a dioxane substituted with C_{1-6}alkyl; tetrahydropyran; a tetrahydropyran substituted with C_{1-6}alkyl; pyrrolidinyl; pyrrolidinyl substituted with one or two substituents each independently selected from halo, hydroxy, cyano, or C_{1-6}alkyl; pyridinyl; pyridinyl substituted with one or two substituents each independently selected from halo, hydroxy, cyano, C_{1-6}alkyl; pyrimidinyl; pyrimidinyl substituted with one or two substituents each independently selected from halo, hydroxy, cyano, C_{1-6}alkyl, C_{1-6}alkyloxy, amino and mono and di(C_{1-6}alkyl)amino; pyridazinyl; pyridazinyl substituted with one or two substituents each independently selected from hydroxy, C_{1-6}alkyloxy, C_{1-6}alkyl or halo; pyrazinyl; pyrazinyl substituted with one ore two substituents each independently selected from halo, hydroxy, cyano, C_{1-6}alkyl, C_{1-6}alkyloxy, amino, mono- and di(C_{1-6}alkyl)amino and C_{1-6}alkyloxycarbonyl;

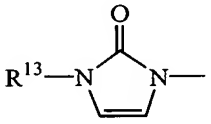
Het^1 can also be a radical of formula



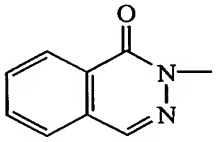
(c-1)



(c-2)

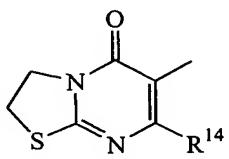


(c-3)

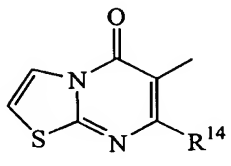


(c-4)

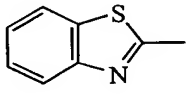
Het^1 and Het^2 each independently can also be selected from the radicals of formula



(d-1)



(d-2)



(d-3)

R^{13} and R^{14} each independently are hydrogen or C_{1-4}alkyl.

2. A compound as claimed in claim 1 wherein the -OR^4 radical is situated at the 3-position of the central piperidine moiety having the trans configuration.

3. A compound as claimed in claim 1 wherein the -OR^4 radical is situated at the 4-position of the central piperidine moiety.

4. A compound as claimed in any of claims 1 to 3 wherein L is C_{3-6}cycloalkyl or C_{2-6}alkenyl; or L is a radical of formula (b-1), wherein each Alk is C_{1-6}alkanediyl, and R^6 is hydrogen, hydroxy, cyano, amino, C_{1-6}alkylsulfonylamino, C_{3-6}cycloalkyl or Het^1, wherein Het^1 is tetrahydrofuran; dioxolane; dioxolane substituted with C_{1-6}alkyl; tetrahydropyran; pyridazinyl substituted with one or more substituents selected from hydroxy, halo and C_{1-6}alkyl; or a radical of formula (c-1), (c-3) or (c-4) wherein R^{13} is C_{1-4}alkyl; or L is a radical of formula (b-2), wherein Alk is C_{1-6}alkanediyl, X is O, and R^7 is C_{1-6}alkyl or hydroxyC_{1-6}alkyl; or L is a radical of formula (b-2), wherein Alk is C_{1-6}alkanediyl, R^7 is Het^2 wherein Het^2 is pyrazinyl substituted with C_{1-6}alkyl, and X is NR^8 wherein R^8 is hydrogen or C_{1-6}alkyl; or L is a radical of formula (b-3) wherein Y is a direct bond, and R^9 is C_{1-6}alkyl, hydroxy or C_{1-6}alkyloxy; or L is a radical of formula (b-4) wherein Y is a direct bond, and R^{11} and R^{12} are C_{1-6}alkyl, or R^{11} and R^{12} combined with the nitrogen atom bearing R^{11} and R^{12} form pyrrolidinyl.

5. A compound as claimed in claim 4 wherein L is butyl; propyl substituted with methoxy, methylcarbonyl or 2-methyl-1,3-dioxolane; ethyl substituted with 4-methyl-2-pyridazinone or tetrahydropyranyl; or methyl substituted with tetrahydrofuranyl or tetrahydropyranyl.

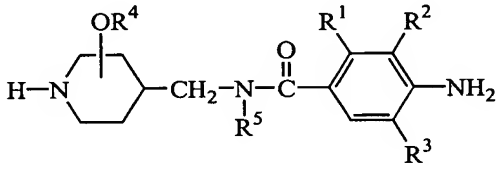
6. A compound as claimed in claim 1 wherein the compound is (trans)-(-)-4-amino-5-chloro-2,3-dihydro-*N*-[[3-hydroxy-1-(3-methoxypropyl)-4-piperidinyl]methyl]-2,2-dimethyl-7-benzofurancarboxamide; a pharmaceutically acceptable acid addition salt or an *N*-oxide form thereof.

7. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 6.

8. A process for preparing a pharmaceutical composition according to claim 7 wherein a therapeutically active amount of a compound according to any of claims 1 to 6 is intimately mixed with a pharmaceutically acceptable carrier.

9. A compound according to any of claims 1 to 6 for use as a medicine.

10. A compound of formula (III)

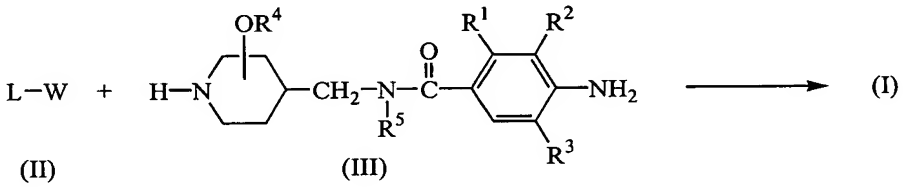


(III);

a pharmaceutically acceptable acid addition salt thereof or a stereochemically isomeric form thereof, wherein R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1 for compounds of formula (I).

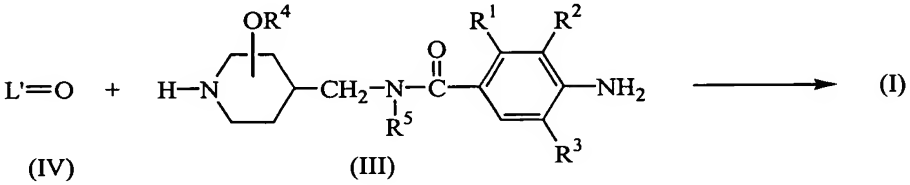
11. A process for preparing a compound of formula (I) wherein

a) an intermediate of formula (II) is *N*-alkylated with an intermediate of formula (III) in a reaction-inert solvent and, optionally in the presence of a suitable base,



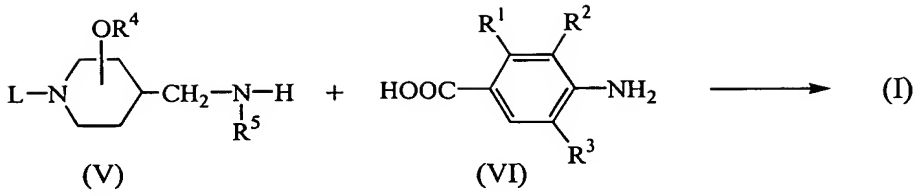
(II) (III) (I)

b) an appropriate ketone or aldehyde intermediate of formula L'=O (IV), said L'=O being a compound of formula L-H, wherein two geminal hydrogen atoms in the C_{1-12}alkanediyl moiety are replaced by =O, is reacted with an intermediate of formula (III);



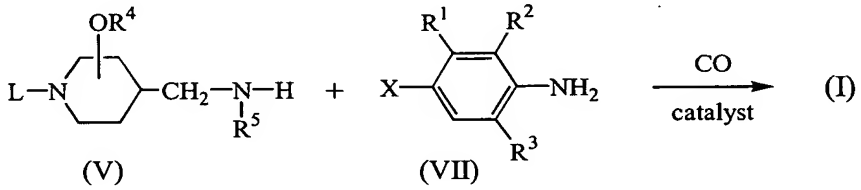
(IV) (III) (I)

c) an intermediate of formula (V) is reacted with an carboxylic acid derivative of formula (VI) or a reactive functional derivative thereof;



(V) (VI) (I)

d) an intermediate of formula (VII), wherein X is bromo or iodo, is carbonylated in the presence of an intermediate of formula (V) in a reaction-inert solvent in the presence of a suitable catalyst and a tertiary amine, and at a temperature ranging between room temperature and the reflux temperature of the reaction mixture;



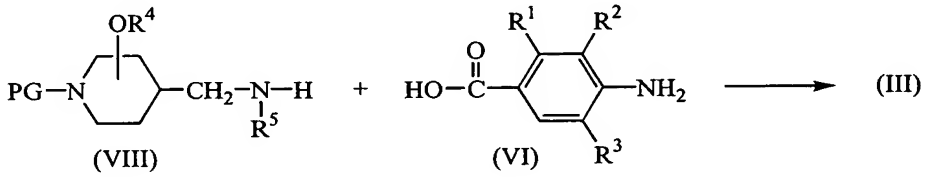
(V) (VII) (I)

wherein in the above reaction schemes the radicals L, R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1 and W is an appropriate leaving group;

e) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

12. A process for preparing a compound of formula (III) wherein

a) an intermediate of formula (VIII), wherein PG is an appropriate protective group, is reacted with an acid of formula (VI), or an appropriate reactive functional derivative thereof, in a reaction-inert solvent and subsequent deprotection of the protecting group PG yielding compounds of formula (III);



(VIII) (VI) (III)

wherein in the above reaction schemes the radicals L, R^1, R^2, R^3, R^4 and R^5 are as defined in claim 1 and W is an appropriate leaving group;

b) or, compounds of formula (III) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (III) is converted into an acid addition salt, or conversely, an acid addition salt of a compound of formula (III) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.